1615

PTO/SB/21 (08-03)
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U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	10/048,033
Filing Date	November 27, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1615
Examiner Name	Not Yet Assigned
Total Number of Pages in This Submission: 25	Attorney Docket Number: NB 2006.01

ENCLOSURES *(check all that apply)*

- ☐ Fee Transmittal Form
  - ☐ Fee Attached
- ☐ Amendment / Reply
  - ☐ After Final
  - ☐ Affidavits/declaration(s)
- ☐ Extension of Time Request
- ☐ Express Abandonment Request
- ☒ Information Disclosure Statement
- ☐ Certified Copy of Priority Document(s)
- ☐ Response to Missing Parts/ Incomplete Application
  - ☐ Response to Missing Parts under 37 CFR 1.52 or 1.53
- ☐ Drawing(s)
- ☐ Licensing-related Papers
- ☐ Petition
- ☐ Petition to Convert to a Provisional Application
- ☐ Power of Attorney, Revocation Change of Correspondence Address
- ☐ Terminal Disclaimer
- ☐ Request for Refund
- ☐ CD, Number of CD(s) _____
- ☐ After Allowance Communication to Group
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☐ Appeal Communication to Group **(Appeal Notice, Brief, Reply Brief)**
- ☐ Proprietary Information
- ☐ Status Letter
- ☒ Other Enclosure(s) *(please identify below)*:

  Form PTO/SB/08a (5 pages), Form PTO/SB/08b (15 pages), 249 references, postcard receipt

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name	Antoinette F. Konski Bingham McCutchen LLP
Signature	Antoinette F Konski
Date	January 11, 2005

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below.

Typed or printed name	Mary R. Zimmerman		
Signature	Mary R Zimmerman	Date	January 11, 2005

PATENT
Docket No. NB 2006.01

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Dated: **January 11, 2005**

Mary R. Zimmerman

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application for:

H. Michael SHEPARD

Serial No.: 10/048,033

Filing Date: November 27, 2002

For: METHODS FOR TREATING THERAPY-RESISTANT TUMORS

Examiner: Not Yet Assigned

Group Art Unit: 1615

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT

Sir:

In accordance with 37 CFR §§ 1.97 and 1.98, the items identified on the attached forms PTO/SB/08a and PTO/SB/08b are being brought to the attention of the Examiner for consideration in connection with the examination of the above-identified patent application. The Examiner is requested to make these documents of record. Copies of the documents are being attached hereto. The Examiner is requested to make these documents of record.

I. Timing of the Information Disclosure Statement:

This Information Disclosure Statement is filed:

☐ With the new patent application submitted herewith (37 C.F.R. § 1.97(a)).

☒ Within three months after the filing date of the application or within three months after the date of entry of the national stage of a PCT application as set forth in 37 C.F.R. § 1.491.

☐ Before the mailing date of a first Office action on the merits. In the event, however, that an Office Action has crossed in the mail with this Information

Disclosure Statement, the Commissioner is hereby authorized to charge Deposit Account No. 50-2518 for any fees required pursuant to 37 C.F.R. §§ 1.17(p) or 1.17(i)(1).

This Information Disclosure Statement is filed:

☐ After the first Office Action and more than three months after the application's filing date; or PCT national stage date of entry filing but, as far as is known to the undersigned, prior to the mailing date of either a final rejection or a notice of allowance, whichever occurs first, and the Commissioner is hereby authorized to charge Deposit Account No.[50-2518] for the fee ($180) set forth in 37 C.F.R. § 1.17(p) and any additional required fees.

This Information Disclosure Statement is filed:

☐ After the mailing date of either a final rejection or a notice of allowance, whichever occurred first, and is accompanied by the fee ($180.00) set forth in 37 C.F.R. § 1.17(i)(1) and a certification as specified in 37 C.F.R. § 1.97(e), as checked below. This document is to be considered as a petition requesting consideration of the Information Disclosure Statement.

The undersigned certifies that:

☐ Each item of information contained in the Information Disclosure Statement was first cited in any communication mailed from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this information disclosure statement.

☐ No item of information contained in this information disclosure statement was cited in a communication mailed from a foreign patent office in a counterpart foreign application or, to the knowledge of the undersigned after making reasonable inquiry, was known to any individual designated in 37 C.F.R. § 1.56(c) more than three months prior to the filing of this Information Disclosure Statement.

II. Copies of the Cited Items:

☒ Copies of all of the items listed on the attached forms PTO/SB/08a and PTO/SB/08b are enclosed.

☐ Copies of only the following items listed on the attached forms PTO/SB/08a and PTO/SB/08b are enclosed:

☐ Copies of all other items not listed above and listed in the attached forms PTO/SB/08a and PTO/SB/08b are not supplied because they were previously cited by or submitted to the Patent Office in a prior Application No. *, filed * and relied upon in this application for an earlier filing date under 35 U.S.C. § 120. See 37 C.F.R. § 1.98(d).

☐ Copies of those items which are marked with an asterisk (**) in the attached Form PTO-1499 were cited in a foreign examination report in a related case. A copy of the search report and the cited references not already of record in this application are attached hereto.

III. Concise Explanation of Relevance:

☒ A concise explanation of relevance of the items listed on forms PTO/SB/08a and PTO/SB/08b is not given.

☐ A concise explanation of relevance of [some of] the items listed on forms PTO/SB/08a and PTO/SB/08b is in the form of an English language copy of a Search Report from a foreign patent office, issued in a counterpart application, which refers to the relevant portions of the references (copy attached).

IV. Related Applications:

☐ Applicants bring to the Office's attention the following related, co-pending application(s):

V. Conclusion:

Citation of the above documents shall not be construed as:

1. an admission that the documents are necessarily prior art with respect to the instant invention;
2. a representation that a search has been made, other than as described above; or
3. an admission that the information cited herein is, or is considered to be, material to patentability as defined in § 1.56(b).

It is respectfully requested that the Examiner indicate consideration of the cited references by returning a copy of the attached forms PTO/SB/08a and PTO/SB/08b with initials or other appropriate marks. The Commissioner is hereby authorized to charge Deposit Account No. 50-2518, billing reference number: 7008282002 for any additional fees required in connection with the filing of this Information Disclosure Statement.

Respectfully submitted,

Dated: January 11, 2005

By: 
Antoinette F. Konski
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 1 of 5

Complete if Known	
Application Number	**10/048,033**
Filing Date	**November 27, 2002**
First Named Inventor	**H. Michael SHEPARD**
Art Unit	**1615**
Examiner Name	**Not Yet Assigned**
Attorney Docket Number	**NB 2006.01**

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Document Number – Number – Kind Code[2] (if known)	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document – Country Code[3] – Number[4] – Kind Code[5] (if known)	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T[6]
	1	DE 32 29 169 A1	02-09-84	De Clercq et al.		
	2	EP 0 311 107 A2	04-12-89	Stichting REGA VZW		
	3	EP 0 311 108 A2	04-12-89	Stichting REGA VZW		
	4	EP 0 316 592	05-24-89	Stichting REGA VZW		
	5	GB 982 776	02-10-65	The Wellcome Foundation		
	6	RO 88451	01-30-86	Antibiotics Enterprise, Iasi		X
	7	WO 89/05817	06-29-89	Nucleic Acid Research Institute		
	8	WO 90/03978	04-19-90	Stichting REGA VZW		
	9	WO 91/17424	11-14-91	Vical, Inc.		
	10	WO 92/19767	11-12-92	Terrapin Technologies, Inc.		
	11	WO 93/06120	04-01-93	University of Rochester		

Examiner's Signature		Date Considered	

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	12	WO 94/03467	02-17-94	Institute of Organic Chemistry & Biochemistry of the Academy of Sciences of the Czech Republic, et al.		
	13	WO 94/22483	10-13-94	Kozak, Alexander		
	14	WO 95/01806	01-19-95	Kondratyev, A.		
	15	WO 95/08556	03-30-95	Amersham International, Inc.		
	16	WO 95/12678	05-11-95	Connors, T. et al.		
	17	WO 96/03151	02-08-96	Springer et al.		
	18	WO 96/07413	04-04-96	University of Georgia Research Foundation & Yale University		

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	19	WO 96/10030	04-04-96	Isis Pharmaceuticals, Inc.		
	20	WO 96/29336	09-26-96	Medical Research Council, University College Cardiff Consultants, Inc. Rega Foundation		
	21	WO 96/33168	10-24-96	Kumiai Chemical Industry Co Ltd et al.		
	22	WO 96/40088	12-19-96	Hostetler, Karl Y.		
	23	WO 96/40708	12-19-96	La Jolla Pharmaceuticals, Inc.		
	24	WO 96/40739	12-19-96	Terrapin Technologies, Inc.		
	25	WO 97/25342	07-17-97	Terrapin Technologies, Inc.		

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	26	WO 97/28179	08-07-97	Fick, James & Israel, Mark		
	27	WO 97/49717	12-31-97	Balzarini et al.		
	28	WO 98/49177	11-05-98	University College Cardiff Consultants Limited		
	29	WO 99/06072	02-11-99	Boehringer Mannheim Corp.		
	30	WO 99/20741	04-29-99	Geron Corporation		
	31	WO 99/23104	05-14-99	The Government of the United States of America represented by The Secretary of Health & Human Services		

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	32	WO 99/37753	07-29-99	NewBiotics, Inc.		
	33	WO 00/18775	04-06-00	University College Cardiff Consultants Limited and Rega Foundation		
	34	WO 00/33888	06-15-00	Dubois, V. et al.		
	35	WO 01/07088	02-01-01	NewBiotics, Inc.		
	36	WO 01/83501	11-08-01	University College Cardiff Consultants Limited and Rega Foundation		
	37	WO 01/85749	11-15-01	University College Cardiff Consultants Limited and Rega Foundation		

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Sheet 1 of 15

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NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T[2]
	1	ABRAHAM et al. "Synthesis and biological activity of aromatic amino acid phosphoramidates of 5-fluoro-2'-deoxyuridine and 1-β-arabinofuranosylcytosine: Evidence of phosphoramidase activity" *J. Med. Chem.* (1996) **39**:4569-4575	
	2	AKDAS et al. "Glutathione S-transferase and multidrug-resistant phenotype in transitional cell carcinoma of the bladder" *Eur. Urol.* (1996) **29(4)**:483-486	
	3	ALMASAN et al. "Genetic instability as a consequence of inappropriate entry into and progression through S-phase" *Cancer Metast. Rev.* (1995) **14**:59-73	
	4	ANDERSEN et al. "Detection of C-ERBB-2 related protein in sera from breast cancer patients" *Acta Oncol.* (1995) **34(4)**:499-504	
	5	ANGLADA et al. "*N,N'*-cyclization of carbodiimides with 2-(bromomethyl)acrylic acid. A direct entry to the system 5-methylene-6*H*-pyrimidine-2,4-dione, A new class of thymine analogues" *J. Heterocyclic Chem.* (July-Aug. 1996) **33**:1259-1270	
	6	ANTELMAN et al. "Inhibition of tumor cell proliferation in vitro and in vivo by exogenous $p110^{RB}$, the retinoblastoma tumor suppressor protein" *Oncogene* (1995) **10**:697-704	
	7	ASAKURA and ROBINS, "Cerium(IV) catalyzed iodination at C5 of uracil nucleosides" *Tetrahedron Lett.* (1988) **29(23)**:2855-2858	
	8	ASAKURA and ROBINS "Cerium(IV)-mediated halogenation at C-5 of uracil derivatives" *J. Org. Chem. (1990)* **55**:4928-4933	
	9	AYISI et al. "Comparison of the antiviral effects of 5-methoxymethyldeoxyuridine-5'-monophosphate with adenine arabinoside-5'-monophosphate" *Antivir. Res.* (1983) **3**:161-174	
	10	BAGSHAWE "Antibody-directed enzyme prodrug therapy: A review", *Drug Develop. Res.* (1995) **34(2)**:220-230	
	11	BAJETTA et al. "A pilot safety study of capecitabine, a new oral fluoropyrimidine, in patients with advanced neoplastic disease" *Tumori* (1996) **82**:450-452	
	12	BALZARINI et al. "Incorporation of 5-substituted pyrimidine nucleoside analogues into DNA of a thymidylate synthetase-deficient murine FM3A carcinoma cell line" *Meth. Find. Exp. Clin. Pharmacol.* (1985) **7(1)**:19-28	
	13	BALZARINI et al. "Thymidylate synthase is the principal target enzyme for the cytostatic activity of (*E*)-5-(2-bromovinyl)-2'-deoxyuridine against murine mammary carcinoma (FM3A) cells transformed with the herpes simplex virus type 1 or type 2 thymidine kinase gene" *Mol. Pharmacol.* (1987) **32**:410-416	

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Examiner Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T[2]
	14	BALZARINI et al. "Differential mechanism of cytostatic effect of (*E*)-5-(2-bromovinyl)-2'-deoxyuridine , 9-(1,3-dihydroxy-2-propoxymethyl)guanine, and other antiherpetic drugs on tumor cells transfected by the thymidine kinase gene of herpes simplex virus type 1 or type 2" *J. Biol. Chem.* (1993) **268(9)**:6332-6337	
	15	BALZARINI et al. "Anti-HIV and anti-HBV activity and resistance profile of 2',3'-dideoxy-3'-thiacytidine (3TC) and its arylphosphoramidate derivative CF 1109" *Biochem. Biophy. Res. Co.* (1996) **225**:363-369	
	16	BALZARINI et al. "Conversion of 2',3'-dideoxyadenosine (ddA) and 2',3'-didehydro-2',3'-dideoxyadenosine (d4A) to their corresponding aryloxyphosphoramidate derivatives markedly potentiates their activity against human immunodeficiency virus and hepatitis B virus" *FEBS Lett.* (1997) **410**:324-328	
	17	BANERJEE et al. "Molecular mechanisms of resistance to antifolates, a review" *Acta Biochim. Pol.* (1995) **42(4)**:457-464	
	18	BANERJEE et al. "Role of E2F-1 in chemosensitivity" *Cancer Res.* (Oct. 1, 1998) **58**:4292-4296	
	19	BARBATO, et al. "Synthesis of bridged pyrimidine nucleosides and triazo [4,3-c] pyrimidine nucleoside analogues" *Nucleos. Nucleot.* (1991) **10(4)**:853-866	
	20	BARBOUR et al. "A naturally occurring tyrosine to histidine replacement at residue 33 of human thymidylate synthase confers resistance to 5-fluoro-2'-deoxyuridine in mammalian and bacterial cells" *Mol. Pharmacol.* (1992) **42**:242-248	
	21	BARR "Inhibition of thymidylate synthetase by 5-alkynyl-2'-deoxyuridylates" *J. Med. Chem.* (1981) ***24*(12)**:1385-1388	
	22	BARR et al. "Thymidylate synthetase-catalyzed conversions of *E*-5-(2-bromovinyl)-2'-deoxyuridylate" *J. Biol. Chem.* (1983) **258(22)**:13627-13631	
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Sheet 3 of 15

Complete if Known	
Application Number	10/048,033
Filing Date	November 28, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1615
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2006.01

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Filing Date	**November 28, 2002**
First Named Inventor	**H. Michael SHEPARD**
Art Unit	**1615**
Examiner Name	**Not Yet Assigned**
Attorney Docket Number	**NB 2006.01**

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Filing Date	**November 28, 2002**
First Named Inventor	**H. Michael SHEPARD**
Art Unit	**Not Yet Assigned**
Examiner Name	**Not Yet Assigned**
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Art Unit	1615
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2006.01

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Sheet 9 of 15

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Application Number	**10/048,033**
Filing Date	**November 28, 2002**
First Named Inventor	**H. Michael SHEPARD**
Art Unit	**1615**
Examiner Name	**Not Yet Assigned**
Attorney Docket Number	**NB 2006.01**

NON PATENT LITERATURE DOCUMENTS

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Sheet 10 of 15

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Filing Date	**November 28, 2002**
First Named Inventor	**H. Michael SHEPARD**
Art Unit	**1615**
Examiner Name	**Not Yet Assigned**
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Art Unit	**1615**
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Art Unit	**1615**
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Filing Date	November 28, 2002
First Named Inventor	H. Michael SHEPARD
Art Unit	1615
Examiner Name	Not Yet Assigned
Attorney Docket Number	NB 2006.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T[2]
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	206	WATAYA et al. "trans-5-(3,3,3-trifluoro-1-propenyl)-2´-deoxyuridylate: A mechanism-based inhibitor of thymidylate synthetase" *J. Med. Chem.* (Apr. 1979) **22(4)**:339-340	
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